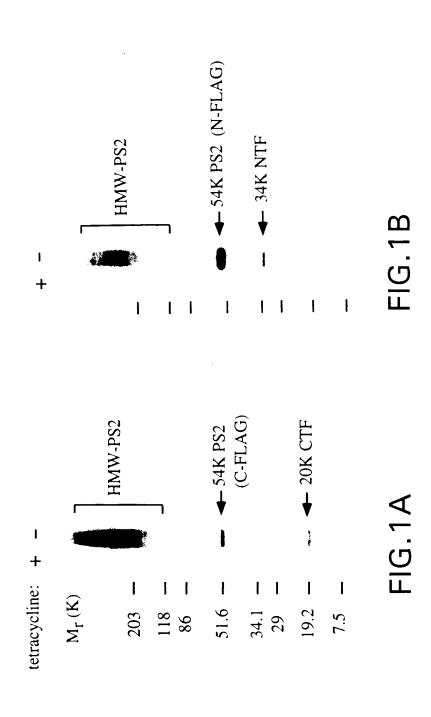
Appl. No. 09/065,902,; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;
Inventors: TANZI and KIM; Tel. 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



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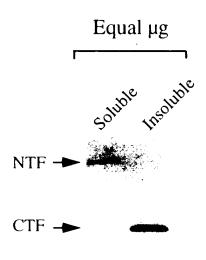
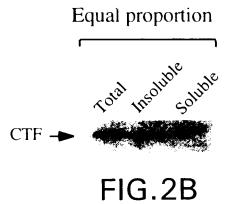


FIG.2A



Appl. No. 09/065,902;; Group Art Unit: 1644

Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel: 202/371-2600

Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

hrs 0 6 12 24 48 72

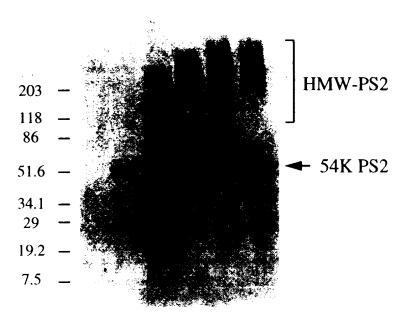


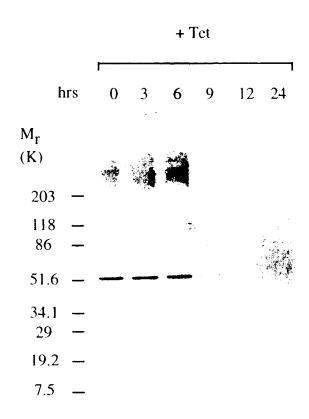
FIG.3A

hrs 0 6 12 24 48 72



FIG.3B

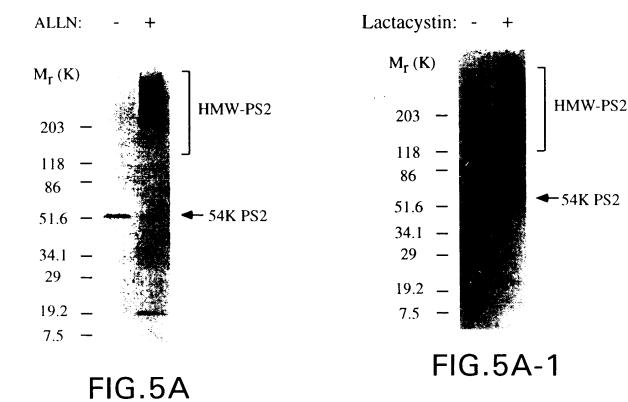
Appl. No. 09/065,902.; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC; ;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title. Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



WT FIG.4A

FIG.4B

Appl. No. 09/065,902;; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC,;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



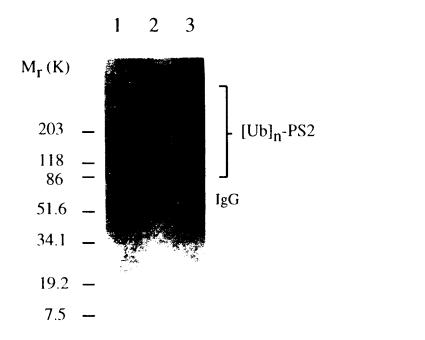
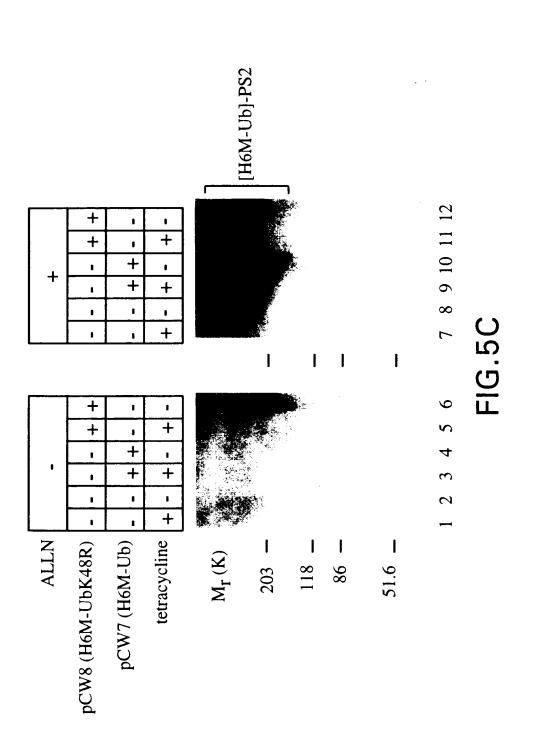


FIG.5B

Appl. No. 09/065,902;; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel. 202/371-2600
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Appl. No. 09/065,902;; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

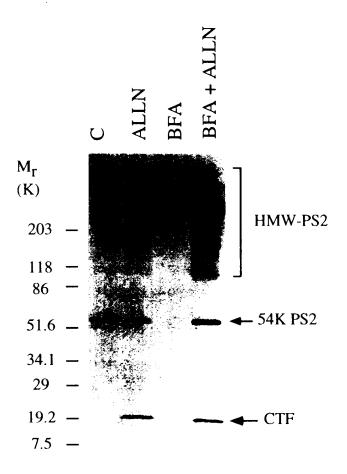


FIG.6

Appl. No. 09/065,902.; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC; ;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

	1	2	tet:	+	_		
$M_{r}(K)$			$M_{r}(K)$				
118 <b>-</b> 86 <i>-</i>			203 —		Sa a sa		
51.6 -	_		118 — 86 —				
34.1 <b>-</b> 29 <b>-</b>	- *		51.6—			- 54K PS2	
19.2 -			34.1 — 29 —			e f	
7.5 -	-		19.2 —		_ = =	$\leq \frac{e}{20 \text{K CTF}}$	
α	PS2Loop	αPS2Loop	7.5 —				
		GST-HuPS2	F	FIG.7B			

FIG.7A

- 86 - 51.6 - 34.1

  $M_{r}(K)$  -118 -86 -51.6 -34.1 -29

**-** 19.2

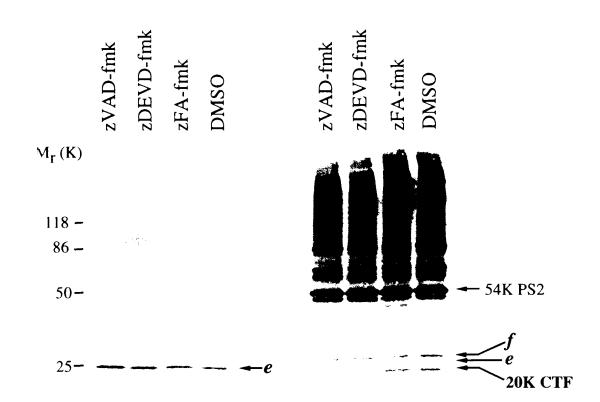
 $\alpha PS2Loop \\$ 

FIG.7C

Ponceau S

FIG.7C-1

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Dkt. No. 0609/4270001/JAG/HLK/PSC; ;
Inventors: TANZI and KIM; Tel. 202/371-2600
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Uninduced

Induced

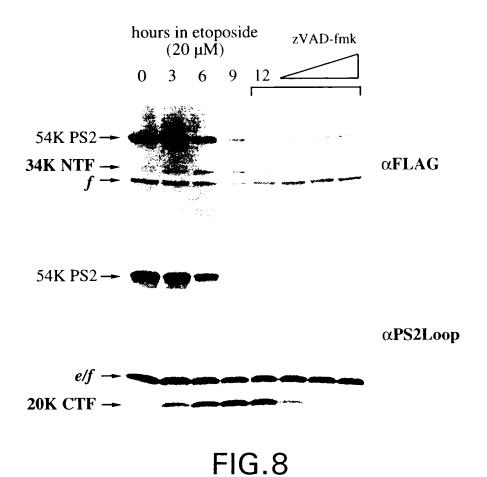
FIG.7D

FIG.7D-1

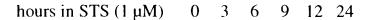
Appl. No. 09/065,902;; Group Art Unit: 1644

Dkt. No. 0609/4270001/JAG/HILK/PSC;;
Inventors: TANZI and KIM; Tel: 202/371-2600

Title Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



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Dkt. No. 0609/4270001/JAG/HLK/PSC; ;
Inventors: TANZI and KIM; Tel. 202371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



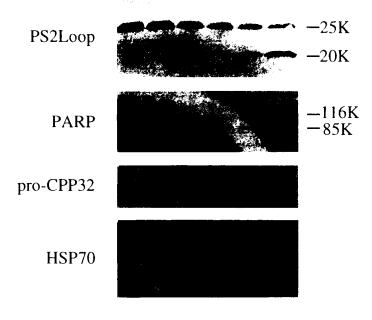


FIG.9A

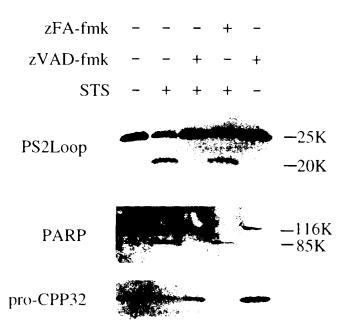
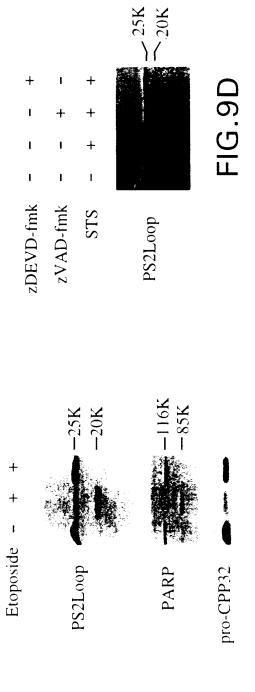


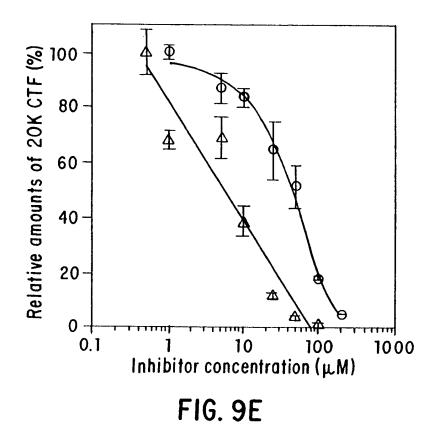
FIG.9B

Appl. No. 09/065,902;, Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;
Inventors: TANZ1 and KIM; Tel. 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



zVAD-fmk -

Appl. No. 09/065,902;; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel: 202371-2600
Title: Purified 20 kDa Presenitin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenitin 2



Normal Cleavage Sites

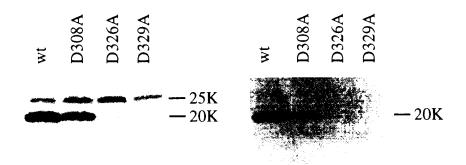
296 Exon 10 323 A B Exon 11

//-PIFPALIYSSAMVWTVGMAKLDPSSQGALQLPYDPEMEEDSYDSFGEPSYPEVFE // PS2

D308A D326A D329A

FIG. 10A

Appl. No. 09/065,902,; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC,;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



αPS2Loop

 $\alpha FLAG$ 

FIG.10B

Appl. No. 09/065,902.; Group Art Unit: 1644

Dkt. No. 0609/4270001/JAG/HLK/PSC; ;
Inventors: TANZI and KIM; Tel: 202/371-2600

Title Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

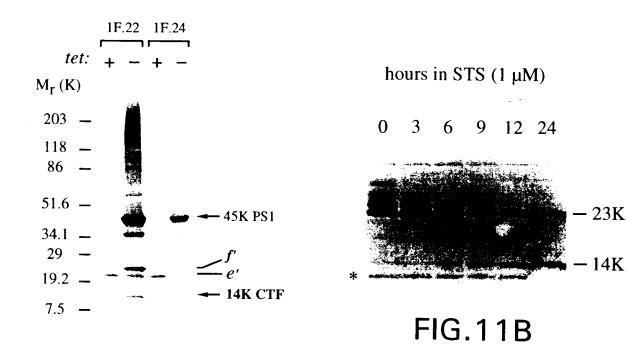


FIG.11A

αPS1Loop

FIG.11C

FIG.11D

Appl. No. 09/065,902;; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

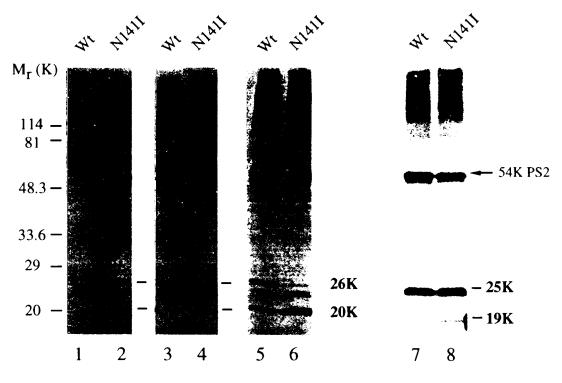


FIG.12A

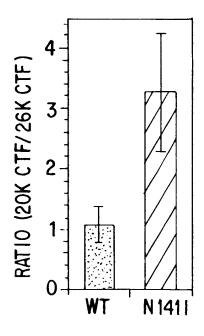


FIG.12B

Appl. No. 09/065,902;; Group Art Unit: 1644 Dkt. No. 0609/4270001/JAG/HI K/PSC; Inventors: TANZI and KIM; Tel: 202/371-2600 Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

N1411 (Volga German) and D329A (Caspase Clip Site) N1411 (Volga German) and D329A (Caspase Clip Site) Establishment of Stable CHO Cell Lines Co-expressing APP and PS2 Containing Mutations

Establishment of Stable CHO Cell Lines Co-expressing APP and PS2 Containing

Mutations

N1411/D329A N1411

Clone# 1 7

Normal CTF

Stable

FIG. 13A

← Normal CTF ← Alt. CTF IItIN N1411/D356 ΙM

**Transient** 

FIG. 13B